

## DISCUSSIONS OF PAPERS ON IMMUNOLOGY AND PUBLIC HEALTH

*Chairman:* LEIGHTON E. CLUFF

*Rapporteur:* ARNOLD G. WEDUM

DISCUSSION OF IMMUNOLOGICAL ASPECTS OF AIRBORNE INFECTION: "SOME GENERAL CONSIDERATIONS OF RESPONSE TO INHALATION OF TOXINS," CARL LAMANNA, AND "REACTIONS TO INHALED ANTIGENS," GARDNER MIDDLEBROOK

*Discussant:* Ivan L. Bennett, Jr.

There is need for work on absorption of toxic bacterial products from the respiratory tract. The bacterial endotoxins have not been mentioned in this Conference in this connection.

Experience at Fort Detrick with accidental inhalation of *Serratia marcescens* provides an example of a clinical syndrome of tightness of chest, low fever, malaise, and slight cough that is associated with intrapulmonary deposition and absorption of the bacterial toxins but unaccompanied by multiplication of the bacteria. This situation is not altogether an artificial laboratory phenomenon because inhalation of foreign particles peculiar to certain industries also can produce a similar condition. Two examples will be given:

- 1) In certain phases of the cotton textile industry, employees inhale significant amounts of raw cotton fiber. At the end of a day's work, a new employee characteristically will have chills and fever. After a few days, symptoms no longer appear at the end of a day, owing to the acquisition of tolerance. There is good reason to believe that the symptoms result not from the cotton fiber but from absorption of endotoxin derived from bacteria on the inhaled fibers. These bacteria are classified in the genus *Aerobacter*.

- 2) In various industries a febrile illness may arise following inhalation of lead and zinc fumes. Studies have shown that these fumes facilitate the absorption of bacterial toxins from the respiratory tract.

There is considerable need for investigation of the site of entry and the mechanism of penetration of microorganisms in the respiratory tract. In addition, much must be learned of the transport of microorganisms and the host-parasite relationships and interactions that influence the course of inhalation infection. Until such informa-

tion is obtained, there is less need for investigation of aerosolized dead vaccines.

Dr. Wright commented that the ciliated cells of the respiratory tract do not seem to be cemented together, and penetration between these cells of microorganisms or toxins to the basement membrane may be important in providing an opportunity for invasion.

Dr. Middlebrook stated that study of a variety of mycobacteria in animals after aerosol challenge, followed by extensive culturing of the nose and other portions of the respiratory tract, and of the internal organs, shows:

- 1) The more attenuated the organisms, the greater is the tendency of the organism to be carried to the mediastinal nodes in a day or so.

- 2) The more virulent the organism, the greater is the tendency for the organisms to remain (be fixed) in the initial site of deposition and to multiply there.

- 3) The leukocytes probably can carry the less virulent organisms to the lymph nodes.

- 4) When a few tubercle bacilli escape being killed by isoniazid used prophylactically, the resultant pulmonary lesions are not in the parenchyma of the lung but are in the lymph nodes. It is postulated that the organisms escaping the full effect of drug therapy for 10 days become mature and torpid. The extent of this maturity may determine how far the organisms are carried in the body before they multiply. The spores of anthrax seem to represent a similar situation.

A question was raised by Dr. McDermott. When BCG is tagged with a radioisotope and injected subcutaneously, the bacilli are rapidly disseminated throughout the body of the animal. If an even less virulent mycobacteria were used, would dissemination be slower? Dr. Middlebrook answered that when BCG is inoculated by aerosol, the organisms do not go beyond the mediastinal nodes to multiply in other organs until after about 2 weeks.

Dr. Lamanna stated that he felt intuitively that the respiratory tract, at different levels, permits entry into the body of varying amounts of toxins. There is no information, however, indicat-

ing how and where toxin penetrates the broncho-pulmonary system.

DISCUSSION OF: PUBLIC HEALTH IMPLICATIONS OF AIRBORNE INFECTION: "PHYSICAL ASPECTS," WILLIAM A. PERKINS AND L. M. VAUGHAN, AND "MEDICAL ASPECTS," ALEXANDER D. LANGMUIR

*Discussant:* Harold Glassman

This Conference has thus far been concerned with: (i) concepts and methods of experimental airborne infection, and (ii) consideration of these concepts in relation to naturally occurring disease phenomena.

Dr. Perkins has significantly enlarged our horizons by his lucid discussion of the physical factors controlling the behavior of an aerosol as it is carried downwind by the atmosphere. Many of the illustrations which he used are based on studies with nonliving, fluorescent particles of zinc cadmium sulfide. The applicability of these studies to the behavior of microbial aerosols is theoretically sound and supported by direct experimental evidence using the spores of *Bacillus globigii* and sampling over a range of 1½ miles from the source of dissemination.

The concept of travel of microorganisms as aerosol clouds can be simplified and integrated by classifying microbial aerosols under three headings based upon distance of movement from their source: (i) micro-range, for travel up to 50 ft; (ii) meso-range, for travel up to 1 mile; and (iii) macro-range, for travel beyond one mile (under some conditions may extend to hundreds of miles). Illustrative examples for each of these headings are evident from the discussions at this Conference, e.g., Eichenwald's "cloud babies" in the micro-range, Riley's hospital sampling in the meso-range, and the Q fever epidemic, cited by Dr. Langmuir, in the macro-range. The same physical laws apply to the travel of microbial aerosols irrespective of the distance involved. The infectivity of these aerosols is determined by such considerations as their source strength, particle-size distribution, and environmental factors (humidity, temperature, solar radiation). The development of the rotating drum apparatus, described earlier in this Conference by Mr. Wolfe, has made it possible to investigate microorganisms resident in the aerosol state for many hours, equivalent to travel

in the extremes of the macro-range. This technique has been used for such a short time that the available data are not nearly as comprehensive as are desired. Furthermore, one must keep in mind that these studies are performed in an enclosed chamber and parallel experimentation in the field is urgently needed. Keeping these reservations in mind, however, it is of interest to note that:

1) Studies during 30 hr of the viability of microbial aerosols demonstrated a markedly superior survival capacity for *Staphylococcus albus* when compared with *Pseudomonas pseudomallei*. The latter exhibited a corresponding superiority to *Pasteurella pestis* (1).

2) The recovery of viable *Brucella suis* is essentially 100% after residence in the aerosol state for 6 hr at 83% relative humidity and 45 F. In contrast, approximately 11% of *Pasteurella tularensis* were viable under the same conditions. Furthermore, long residence in the aerosol state diminished the infectivity of the latter microorganism (2).

3) The survival of both of the latter bacteria is diminished if the relative humidity is decreased or the temperature increased.

4) Vaccinia virus and influenza virus are highly stable. Recovery of approximately 60% of viable microorganisms is observed after residence in the aerosol state for 23 hr at 20% relative humidity and 45 to 50 F.

5) The survival of each of these viruses is diminished if the relative humidity is increased (note contrast to bacteria cited above) or the temperature increased. Unpublished data in the above subparagraphs were kindly made available by G. J. Harper.

Dr. Riley drew attention to the importance of:

1) The average infected person as a disseminator of infection, in contrast to the specialized person represented by the "cloud baby" or the exceptionally contagious spreader of tuberculosis or plague. Although disseminators undoubtedly exist, their elimination presents a formidable public health problem. This approach is, therefore, likely to be of limited value in preventive medicine.

2) The outdoor atmosphere, where dilution and solar radiation are comparatively effective safeguards, in contrast to the indoor atmosphere.

3) Environmental control vs. immunological control. The deliberations of this Conference have been aimed principally at individual control.

The focus on disseminators may lure us away from environmental control. How much dependence can be placed on vaccines for the common acute respiratory diseases, considering the length of time that immunity by vaccination may be effective?

Dr. Davenport stated that in relation to the use of vaccines as protection against respiratory disease, investigation indicates that there is great potentiality in combined respiratory virus vaccines. One "package vaccine" may include many virus antigens.

Dr. McDermott called attention to one aspect of respiratory disease that has not been mentioned and that could be discussed profitably; namely, as city dwellers move in large numbers to the suburbs, diseases usually associated with farmers arise in persons considered urban in habit. Histoplasmosis is an example.

Students of tuberculosis now realize that there is still much unknown about just how this disease is spread. The relative importance is undetermined, for the "dangerous disseminator" so well described by Dr. Langmuir, for the "average patient" so much emphasized by Dr. Riley, and for environmental factors such as ventilation, housing, and sunlight.

Dr. McDermott quoted Dr. Smith as saying that development of the concept of determination of ecological growth requirements of the pathogenic saprophyte *C. immitis* should not be discouraged. Indeed, from the applied aspect, source and environmental control in limited areas *could* complement dust control. However, in coming to grips with the total problem of coccidioidomycosis, Dr. Smith adds, this concept is *not* realistic.

As was indicated in the discussion previously, we also favor the concept of "pockets" of multiplication of *C. immitis*. However, if real, these pockets extend over literally hundreds of thousands of square miles of the most rugged terrain. To identify these pockets, to modify the critical conditions (whatever these may be) and *per-*

*manently* prevent the multiplication of *C. immitis* is hopeless. "Nature" is on the side of the "saprophyte" and, accepting the inevitable, we continue by draining the fangs of "pathogenicity."

Dr. Furcolow stated that the importance of localization in histoplasmosis should not be underestimated in those instances in which the starling is the principal factor. These birds may congregate in vast flocks of 100,000 to more than a million. In such cases, localized control may provide significant results.

Dr. Langmuir added that the environmental control of airborne infection has its specific applications, but it can never be as important as the environmental control of water and food. The air is ubiquitous; water and food are highly restricted and therefore subject to economic control.

The concept of the "dangerous disseminator" offers us a new approach to the possible control of airborne infections such as tuberculosis. We should seek a better understanding of the special circumstances necessary to produce those small diameter microbe-bearing particles that are crucial to infection through the terminal alveolus. Fruitful results might appear if we knew what act, characteristic, or condition of the patient produced such fine-particle infective aerosols. For instance, does a particular type of sputum or nasal discharge characterize the "spreader"? Does one type of speech, enunciation, or act of singing produce more small particles than another?

#### LITERATURE CITED

1. GOLDBERG, L. J., H. M. S. WATKINS, E. E. BOERKE, AND M. A. CHATIGNY. 1958. The use of a rotating drum for the study of aerosols over extended periods of time. *Am. J. Hyg.* **68**:85-93.
2. SCHLAMM, N. A. 1960. Detection of viability in aged or injured *Pasterurella tularensis*. *J. Bacteriol.* **80**:818-822.